

REMARKS

Upon entry of the present amendment, Claims 1-11, 15, and 17-20 will be pending in the present application. Claims 1, 2 and 9 have now been amended. Support for the amendments can be found throughout the specification, for *e.g.*, at par. spanning p. 2-3, p. 4, 1st. par, and Example 5, p. 10-12. No new matter was added.

Claim 16 was previously canceled. Claims 12, 13 and 14 have now been canceled without prejudice. Applicant reserves the right to pursue these claims in a continuation application.

Reconsideration of the present application is respectfully requested.

35 USC 1.132 Declarations

The Examiner states that the papaya products (CARICOL® (C), a papaya puree preparation prepared according to the method recited in Applicant's claims, and reference papaya puree (P)), tested in the Wutschitz declaration and described in the Erhard declaration, are not comparable, and that the Wutschitz declaration is not commensurate in scope with the invention as claimed.

The Examiner refers to the reference papaya puree (P), a customary papaya fruit pulp (prepared by a customary method known in the art), as a "generic, uncooked, bottled papaya product." Applicant respectfully submits that as explained in the Erhard declaration, the reference papaya pulp (P) was pasteurized "by heating the bottled papaya pulp (P) for around 20 minutes at 90⁰C and letting it cool down to room temperature for a further 20 minutes." (*see*, Erhard Declaration filed October 13, 2010, p. 3; emphases added; of record). The reference papaya pulp (P) was subjected to the "action of heat," and is therefore representative of a papaya puree preparation in the art.

It is well established that "[a]pplicant cannot be required to compare the claimed invention with an invention suggested by a combination of references relied upon by the Examiner in a 103 rejection. This would be "requiring comparison of the results of the invention with the results of the invention." *In re* Chapman 357 F.2d 418 USPQ 711

(CCPA 1966).” (*see*, MPEP 716.02(e)). Thus, the comparison of CARICOL® (C) and reference papaya puree (P)) in the Wutschitz declaration is appropriate.

The clinical studies presented in the Wutschitz declaration show CARICOL®, a papaya puree preparation prepared according to the method recited in Applicant’s claims, has unexpectedly superior health properties in comparison to other known papaya puree preparations. As discussed below, the prior art fails to teach or suggest that a papaya puree prepared according to Applicant’s invention would have resulted in a preparation with the health benefits recited in Applicant’s present claims.

Rejection Under 35 U.S.C. § 103

(A) Rejection over Wolff (US 4089985)

Claims 1-3, 5-7, 15, 18 and 19 stand rejected over as obvious over Wolff (US 4089985) (hereinafter “Wolff”) on the ground that Wolff teaches a hot blended papaya preparation at 91⁰C-99⁰C and discloses cooling and pasteurization. The Examiner believes that a person of skill in the art would have been motivated to modify Wolff “by modifying routinely determinable parameters” to arrive at Applicant’s present claims. Applicant respectfully traverses the rejection.

Applicant respectfully submits that obviousness analysis under U.S. Patent Law requires both: (i) a finding that there was some motivation or reason, either in the reference or in the general knowledge in the art, to modify the reference or to combine reference teachings; and (ii) finding that there was reasonable expectation of success. For the reasons explained below, Wolff fails to satisfy this requirement.

Claim 1 has been amended to recite cooking time of at least 2 hours, and that the “puree preparation has prophylactic and/or therapeutic properties.” Wolff fails to teach or suggest beneficial health effects of his preparation. The deficiency of Wolff with respect to this key feature has been acknowledged by the Examiner. The Examiner states Wolff “is silent about the method of using papaya product to treat certain disorders.” [Office Action mailed April 2, 2009, p. 8, 1st par., of record]. For the reasons discussed below, a

person of skill in the art reading Wolff would not have had any reason to modify Wolff to prepare and to administer the recited papaya puree preparation with any reasonable expectation of success of achieving the beneficial health effects recited in Applicant's present claims.

First, Wolff was concerned with characteristics such as taste, smell, color, appearance and shelf life of his papaya juice preparation (*see*, Wolff, column 2, 1st full par.). As stated above, Wolff does not teach or suggest any health effect(s) of his preparation. Moreover, such effects could not have been gleaned by a skilled individual based on knowledge in the art *vis-à-vis* loss of papain activity at temperatures > 85⁰C (*i.e.*, thermal inactivation). This discussed in detail below.

Regarding Wolff's method, the Examiner states that Wolff's heated blending reached temperatures of 91⁰C-99⁰C for about 26 minutes [Office Action mailed December 8, 2010, par. spanning p. 12-13]. As discussed in the specification, as of the effective filing of the present application, it was well known in the art that among other ingredients, papaya contains papain to which beneficial medicinal properties are known to be attributed (*see*, specification, *e.g.*, p. 2, par. 2-5). However, it was well-acknowledged in the art that papain is inactivated when subjected to temperatures above 85⁰C (*see*, specification p. 5, 2nd full par.). Applicant unexpectedly discovered high papain activity in CARICOL®, a puree preparation prepared according to the method recited in the present claims. This is discussed in detail by the enclosed declaration by Dr. Concetta Giuliani, hereinafter "Giuliani declaration" (*see*, Attachment A).

As discussed in the Giuliani declaration, Winnick *et al.* showed that at 83⁰C, papain is rapidly (<10 minutes) inactivated (*see*, Attachment 2 to Giuliani declaration- Winnick *et al.*). Further, Winnick *et al.* also note that the heat inactivation of papain could not be reversed by cooling (*see*, Winnick *et al.*, p. 311, abstract, 2nd. par.).

Dr. Giuliani discusses that the papaya puree preparation recited in Applicant's present claims is cooked by heating up to a boiling temperature of approximately 212⁰F (100⁰C) and held at that temperature throughout the length of the cooking step (*i.e.*, at least 2 hours) (*see*, Attachment A-Giuliani declaration, par. 11). Surprisingly, despite the

lengthy boiling process, a 4-fold increment in papain activity was observed in a CARICOL® sample, a papaya puree preparation prepared according to the method recited in Applicant's present claims, when compared to a reference papaya puree preparation which was pasteurized at 90°C for 20 minutes (*see*, Giuliani declaration, par. 12 and Attachment 3 to declaration). This result was unexpected in view of the knowledge in the field (*see*, Giuliani declaration, par. 13-14). Wolff fails to teach or suggest this unexpected benefit.

With respect to the cooling step recited in Applicant's present claims, the Examiner acknowledges that Wolff "is silent about the time of cooling as recited in claims 1 and 3," but states that it would be "routinely determinable by one of ordinary skill in the art." [Office Action mailed December 8, 2010, p. 5, 1st par.]. The specification emphasizes the importance of the cooling process and states that "the supply of oxygen is important during the cooling process" (*see*, specification, par. spanning p. 2-3). Applicant submits that the cooling conditions recited in the present claims are not merely to "cool a hot product faster" as the Examiner states (*see*, Office Action mailed December 8, 2010, p. 5, 1st par. last sentence). Applicant has discovered surprising beneficial health properties of the puree preparation of the invention, and the specification notes that such property "will not occur, or occur only to an extremely slight extent, if said cooking and cooling times are not observed" (*see*, specification, p. 2, par. 7). The beneficial health properties of the puree preparation of the invention are illustrated in Examples 3-7 of the present specification (*see*, specification. p. 8-15) and in the Wutschitz declaration filed September 23, 2009 (of record).

Thus, in view of the above knowledge in the art with respect to thermal kinetics of papain, a person of skill in the art reading Wolff would have not have had any reason to modify Wolff by "routinely optimizing" conditions so as to increase the temperature and time of heat exposure, and have any reasonable expectation of success at arriving at a puree preparation with prophylactic and/or therapeutic properties recited in Applicant's present claims.

With respect to claims 15 and 19, which recite a puree preparation made according to Applicant's novel method, the unexpected presence of high papain activity in the preparation structurally differentiates the puree preparation of the invention from other papaya preparations which do not achieve the recited beneficial health properties.

Thus, for the reasons discussed above, Wolff fails to render claims 1-3, 5-7, 15, 18 and 19 obvious. Withdrawal of the rejection is respectfully requested.

(B) Rejection over Wolff in view of Swensen (US 5840356)

Claim 4 stands rejected as obvious over Wolff in view of Swensen (US 5840356) (hereinafter "Swensen") on the ground that Swensen teaches that acidic pH helps to preserve fruit (*e.g.*, papaya) purees. Applicant respectfully traverses the rejection.

Applicant respectfully submits that Swensen was concerned with preservation and shelf-stability of his fruit puree. Further, Swensen discourages use of heat in his process and states that "increased temperatures can impart stress on the food product, reducing its integrity." Nowhere does Swensen teach or suggest usefulness of his fruit (papaya) puree for achieving beneficial health effects or provide any guidance for processing his puree preparation to achieve such effects. Thus, Swensen fails to remedy Wolff's deficiencies (discussed above), and therefore the combined teachings of Wolff and Swensen cannot make Applicant's claim 4 obvious.

Withdrawal of the rejection is respectfully requested.

(C) Rejection over Wolff in view of Dawson, Chandalia and Imao.

Rejection over Wolff in view of Dawson:

Claims 8-14 stand rejected as obvious over Wolff in view of Dawson on the ground that Dawson discloses medicinal properties of papaya and its beneficial uses to treat certain disorders. Applicant respectfully traverses the rejection.

Regarding Dawson, the Examiner points to a statement in Dawson referring to papain that "although it is a protein, this enzyme is not damaged by heat" (*see*, Dawson, p. 2; of record). Applicant respectfully submits that as discussed above, a person of skill

in the art would have known that papain is inactivated at temperature $>85^{\circ}\text{C}$. Winnick *et al.*, showed that “papain is by far the most resistant to heat inactivation” in comparison to the other plant enzymes he studied (*i.e.*, bromelin and asclepain), however papain is thermally inactivated (destroyed) at $75-83^{\circ}\text{C}$. (*see*, Winnick, *et al.*- Attachment 2 to Giuliani, p. 306, 1st par.; p. 303, Fig. 1). This point is further illustrated in recent studies by Xue *et al.*, who observed that maximum activity of immobilized native papain was obtained at 80°C , but decreases dramatically between 80°C - 90°C (*see*, Attachment B: Xue *et al.*, Immobilization of modified papain with anhydride groups on activated cotton fabric, *Appl. Biochem. Biotechnol.* (2010), 160:109-121; p. 116, 2nd full par.; p. 117, Fig. 4).

Thus, for the reasons discussed above with respect to the rejection over Wolff, the combined teachings of Wolff and Dawson fail to render Applicant’s claims 8-11 obvious. Withdrawal of the rejection is respectfully requested.

Rejection over Wolff in view of Chandalia and Imao.

Claims 12-14 have been canceled, thus the rejections over Chandalia and Imao are now moot.

(D) Rejection over Wolff in view of JP08056562 to Nakayama

Claims 17 and 20 stand rejected over Wolff in view of Nakayama on the ground that Nakayama teaches a cooked papaya product containing 25-35% sugar, which falls within the range recited in the above claims. Applicants respectfully traverse the rejection.

Applicant respectfully submits that for the reasons discussed above, Nakayama fails to remedy Wolff’s deficiencies, and thus the combined teachings of Wolff and Nakayama cannot render claims 17 and 20 obvious. Withdrawal of the rejection is respectfully requested.

Unexpected benefit must be given weight:

As discussed above, Applicant has shown that the papaya puree preparation of the invention has unexpectedly high papain activity and unexpectedly superior health properties compared to other papaya preparations.

Addressing Examiner's statement in the Office Action mailed April 15, 2010, p.11, point 5) that "features upon which applicant relies [] are not recited in the rejected claim(s)," Applicant submits that under the US Patent Law, the Patent Office is required to give weight to the unexpected benefit argument, even when the unexpected benefit is not expressly recited in the claims. In fact, it has long been established that "no law requir[es] that unexpected results relied upon for patentability be recited in the claims." *In re Merchant*, 575 F.2d 865; 197 U.S.P.Q. 785 (CCPA, 1978) (reversing finding of obviousness on the ground that the unexpected results should have been considered by the Examiner and the Board even though they were not recited in the claims.).

Conclusion:

In view of the above remarks, Applicants believe that the application is in condition for allowance. Such action is respectfully requested.

Respectfully submitted,

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